(c) a non-specific immune response enhancer comprising a Ribi Adjuvant system based adjuvant;

and thereby stimulating and/or expanding T cells in a mammal.

REMARKS

Favorable reconsideration of the subject application is respectfully requested in view of the above amendments and the following remarks. Claims 35-37, 57, and 63-69 are pending in the application.

With the above amendment, new claims 104-109 have been added and claims 35, 37, 63, 68, and 69 have been amended for purposes of clarity and to more clearly define certain aspects of the Applicants' invention. It is urged that support for all the above amendments may be found throughout the specification as originally filed and that none of the amendments constitutes new matter. In particular, support for carriers such as microspheres can be found, for example, on page 33, lines 1-13. Support for immune response enhancers and adjuvants can be found, for example, on page 33, line 21-page 34, line 17. It should also be noted that the above amendments are not to be construed as acquiescence with regard to the Examiner's rejections and are made without prejudice to prosecution of any subject matter removed or modified by this amendment in a related divisional, continuation or continuation-in-part application.

Rejection under 35 U.S.C. § 112, first paragraph (written description)

Claims 35, 37, and 63-69 stand rejected under 35 U.S.C. § 112 first paragraph as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. In particular, the Examiner alleges that there is no support in the specification for the recitation of "between 1 and 3 amino acid positions within the immunogenic portion such that the ability of the variant to react with WT1-specific T cell lines or clones is not substantially diminished" and that the claimed invention constitutes new matter. The Examiner claims that there is only support for between 1 and 3 amino acid

substitutions such that the ability of the variant to react with WT1 is enhanced. Additionally, the Examiner maintains that variants of the claimed immunogenic portion are not disclosed in the specification and therefore, the written description in the specification is not commensurate with the scope of the claimed invention.

Applicants respectfully traverse this rejection on the following grounds.

With regard to the claimed invention constituting new matter, Applicants submit that the courts have held that all that is required to comply with the written description requirement is that the specification **reasonably convey** to persons skilled in the art that the inventor had possession of the subject matter claimed. (In re Edwards, 568 F.2d 1349, 1351, 196 USPQ 465, 467 (CCPA 1978) (emphasis added). Applicants submit that the specification clearly describes variants, for example, on page 15, lines 19 - 24, as follows:

> As noted above, a composition may comprise a variant of a native WT1 protein. A polypeptide "variant," as used herein, is a polypeptide that differs from a native polypeptide in **one or more substitutions**, deletions, additions and/or insertions, such that the immunogenicity of the polypeptide is retained (*i.e.*, the ability of the variant to react with antigen-specific antisera and/or T-cell lines or clones **is not substantially diminished** relative to the native polypeptide). (emphasis added)

The specification goes on to further define certain preferred embodiments of a variant in the context of the present invention on page 16, lines 6 - 10 as follows:

> It has been found, within the context of the present invention, that a relatively small number of substitutions (*e.g.*, 1 to 3) within an immunogenic portion of a WT1 polypeptide may serve to enhance the ability of the polypeptide to elicit an immune response. ... Accordingly, within certain preferred embodiments, a WT1 polypeptide comprises a variant in which 1 to 3 amino acid resides within an immunogenic portion are substituted such that the ability to react with antigen-specific antisera and/or T-cell lines or clones is statistically greater than that for the unmodified polypeptide.

Applicants submit that the skilled artisan would readily appreciate in light of this description that the Applicants were indeed in possession of the claimed variants that differ from

the immunogenic portion due to substitutions at between 1 and 3 amino acid positions (*i.e.* one or more) within the immunogenic portion, such that the ability of the variant to react with WT1-specific T cell lines or clones is not substantially diminished.

Nevertheless, without acquiescing to the Examiner's allegations, Applicants have amended the claims without prejudice to remove recitation of substitutions at between 1 and 3 amino acid positions within the immunogenic portion, such that the ability of the variant to react with WT1-specific T cell lines or clones is not substantially diminished. Therefore, this basis for rejection has been obviated and the rejection may be properly withdrawn.

As for the "variant" language of the claims, the Examiner alleges that the specification discloses the peptide of SEQ ID NO:144 as binding HLA-A24 and that the vast majority of other MHC molecules would require amino acid substitutions in SEQ ID NO:144 in order to bind said peptide. The Examiner believes that the nature of said substitutions is not disclosed in the specification. Applicants submit that the specification discloses that SEQ ID NO:144 binds a number of different MHC molecules, including HLA-A24, -B60, -B7, -B8, -B3902, -B5101, -B5102, -CW0301, -CW0602, -CW0702, and various mouse MHC molecules (*e.g.*, page 49, lines 4-14, and Tables V, XIII, XVI-XVII, XXIV, XXVI, XXVII, XXX, XXXII-XXXVII, and XLVI). Given the description in the instant specification (for example, at page 49, lines 4 - 10) and the level of skill in the art at the time of filing, Applicants submit that the skilled artisan would readily appreciate the nature of substitutions necessary for binding of the peptide of SEQ ID NO:144 to these various MHC molecules and the routine nature of identifying said substitutions. For example, MHC peptide-binding motifs were well known in the art at the time of filing. Therefore, the skilled artisan would readily recognize a core structure represented by the epitope of SEQ ID NO:144 and would recognize that substitutions at positions other than the binding residues of 2 and 9 of SEQ ID NO:144, i.e., substitutions that would not be expected to disrupt binding the MHC molecule, would be particularly illustrative substitutions. Applicants submit that the skilled artisan would readily understand, in light of the Applicants' disclosure, the single identifying characteristic common to the claimed variants, *i.e.*, their ability to stimulate T cells specific for SEQ ID NO:144, and would further appreciate the routine nature of the techniques used in their identification. Thus, in view of the Applicants' specification, and the routine and art recognized approaches for the identification and evaluation of variants that are

reactive with antigen-specific T-cells, the person of ordinary skill in the art would recognize that the applicants were indeed in possession of the presently claimed invention as of the filing date of the captioned application.

Nevertheless, in order to expedite prosecution of the present application, and without acquiescing to the Examiner's rejections, Applicants have amended the claims to remove recitation of variant language. Thus, Applicants submit that the present basis for the rejection has been obviated and may be properly withdrawn.

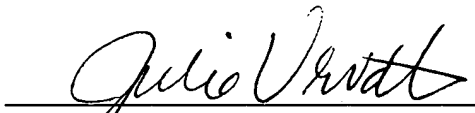
Attached hereto is a marked-up version of the changes made to the specification and claims by the current amendment. The attached page is captioned "**Version With Markings to Show Changes Made.**"

Applicants submit that the claims remaining in the application are now in condition for allowance. Favorable consideration and a Notice of Allowance are earnestly solicited.

Respectfully submitted,

Alexander Gaiger et al.

Seed Intellectual Property Law Group PLLC



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VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the Claims:

New claims 104-109 have been added.

Claims 35, 37, 63, 68, and 69 have been amended as follows:

35. (Twice Amended) A method for enhancing or inducing an immune response in a human patient, comprising administering to a patient a composition comprising:

(a) a WT1 polypeptide consisting of an immunogenic portion of a native WT1 ~~or a variant thereof that differs from the immunogenic portion due to substitutions at between 1 and 3 amino acid positions within the immunogenic portion, such that the ability of the variant to react with WT1-specific T cell lines or clones is not substantially diminished~~, wherein the immunogenic portion consists of the consecutive amino acids of SEQ ID NO:144; and

(b) a physiologically acceptable carrier or excipient;

and thereby enhancing or inducing an immune response specific for WT1 or a cell expressing WT1 in the human patient.

37. (Twice Amended) A method for enhancing or inducing an immune response in a human patient, comprising administering to a patient a composition comprising:

(a) a WT1 polypeptide consisting of an immunogenic portion of a native WT1 ~~or a variant thereof from the immunogenic portion due to substitutions at between 1 and 3 amino acid positions within the immunogenic portion, such that the ability of the variant to react with WT1-specific T cell lines or clones is not substantially diminished~~, wherein the immunogenic portion consists of the consecutive amino acids of SEQ ID NO:144; and

(b) a non-specific immune response enhancer;

and thereby enhancing or inducing an immune response specific for WT1 or a cell expressing WT1 in the human patient.

63. (Twice Amended) A method for stimulating and/or expanding T cells, comprising contacting T cells with a WT1 polypeptide~~,~~ or a polynucleotide encoding a WT1 polypeptide ~~and/or an antigen presenting cell that expresses a WT1 polypeptide~~, wherein said

WT1 polypeptide consists of an immunogenic portion of native WT1~~, or a variant thereof that differs from the immunogenic portion due to substitutions at between 1 and 3 amino acid positions within the immunogenic portion, such that the ability of the variant to react with WT1-specific T cell lines or clones is not substantially diminished~~, wherein the immunogenic portion consists of the consecutive amino acids of SEQ ID NO:144, under conditions and for a time sufficient to permit the stimulation and/or expansion of T cells.

68. (Twice Amended) A method for stimulating and/or expanding T cells in a mammal, comprising administering to a mammal a composition comprising:

(a) one or more of:

(i) a WT1 polypeptide; or

(ii) a polynucleotide encoding a WT1 polypeptide;~~ or~~

~~(iii) an antigen-presenting cell that expresses a WT1 polypeptide;~~

wherein said WT1 polypeptide consists of an immunogenic portion of native WT1~~, or a variant thereof that differs from the immunogenic portion due to substitutions at between 1 and 3 amino acid positions within the immunogenic portion, such that the ability of the variant to react with WT1-specific T cell lines or clones is not substantially diminished~~, wherein the immunogenic portion consists of the consecutive amino acids of SEQ ID NO:144; and

(b) a physiologically acceptable carrier or excipient;

and thereby stimulating and/or expanding T cells in a mammal.

69. (Twice Amended) A method for stimulating and/or expanding T cells in a mammal, comprising administering to a mammal a composition comprising:

(a) one or more of:

(i) a WT1 polypeptide; or

(ii) a polynucleotide encoding a WT1 polypeptide;~~ or~~

~~(iii) an antigen-presenting cell that expresses a WT1 polypeptide;~~

wherein said WT1 polypeptide consists of an immunogenic portion of native WT1~~, or a variant thereof that differs from the immunogenic portion due to substitutions at between 1 and 3 amino acid positions within the immunogenic portion, such that the ability of~~

~~the variant to react with WT1-specific T-cell lines or clones is not substantially diminished~~, wherein the immunogenic portion consists of the consecutive amino acids of SEQ ID NO:144; and

(b) a non-specific immune response enhancer;

and thereby stimulating and/or expanding T cells in a mammal.

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